SDHC gene

succinate dehydrogenase complex subunit C

Normal Function

The *SDHC* gene provides instructions for making one of four subunits of the succinate dehydrogenase (SDH) enzyme. The SDH enzyme plays a critical role in mitochondria, which are structures inside cells that convert the energy from food into a form that cells can use. The SDHC protein helps anchor the SDH enzyme in the mitochondrial membrane.

Within mitochondria, the SDH enzyme links two important cellular pathways in energy conversion: the citric acid cycle (or Krebs cycle) and oxidative phosphorylation. As part of the citric acid cycle, the SDH enzyme converts a compound called succinate to another compound called fumarate. Negatively charged particles called electrons are released during this reaction. The electrons are transferred through the SDH subunits, including the SDHC protein, to the oxidative phosphorylation pathway. In oxidative phosphorylation, the electrons help create an electrical charge that provides energy for the production of adenosine triphosphate (ATP), the cell's main energy source.

Succinate, the compound on which the SDH enzyme acts, is an oxygen sensor in the cell and can help turn on specific pathways that stimulate cells to grow in a low-oxygen environment (hypoxia). In particular, succinate stabilizes a protein called hypoxia-inducible factor (HIF) by preventing a reaction that would allow HIF to be broken down. HIF controls several important genes involved in cell division and the formation of new blood vessels in a hypoxic environment.

The *SDHC* gene is a tumor suppressor, which means it prevents cells from growing and dividing in an uncontrolled way.

Health Conditions Related to Genetic Changes

gastrointestinal stromal tumor

hereditary paraganglioma-pheochromocytoma

More than 30 mutations in the *SDHC* gene have been found to increase the risk of hereditary paraganglioma-pheochromocytoma type 3. People with this condition have paragangliomas, pheochromocytomas, or both. An inherited *SDHC* gene mutation predisposes an individual to the condition, and a somatic mutation that deletes the normal copy of the *SDHC* gene is needed to cause hereditary paraganglioma-pheochromocytoma type 3.

Most of the inherited *SDHC* gene mutations change single protein building blocks (amino acids) in the SDHC protein sequence or result in a shortened protein. As a result, there is little or no SDH enzyme activity. Because the mutated SDH enzyme cannot convert succinate to fumarate, succinate accumulates in the cell. The excess succinate abnormally stabilizes HIF, which also builds up in cells. Excess HIF stimulates cells to divide and triggers the production of blood vessels when they are not needed. Rapid and uncontrolled cell division, along with the formation of new blood vessels, can lead to the development of tumors in people with hereditary paraganglioma-pheochromocytoma.

cancers

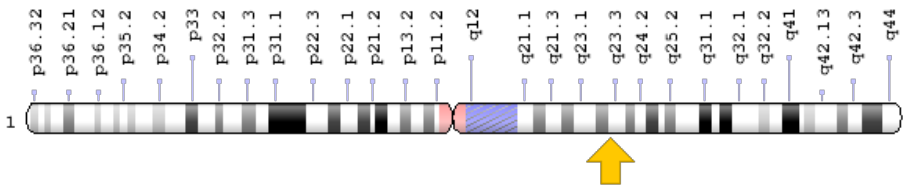
Mutations in the *SDHC* gene have been found in a small number of people with gastrointestinal stromal tumor (GIST), which is a cancer of the gastrointestinal tract. *SDHC* gene mutations have also been identified in people with noncancerous tumors associated with the nervous system called paragangliomas or pheochromocytomas (a type of paraganglioma). Some affected individuals have both paraganglioma and GIST, which is called Carney-Stratakis syndrome. An inherited SDHC gene mutation predisposes an individual to cancer formation. An additional mutation that deletes the normal copy of the gene is needed to cause these forms of GIST and paraganglioma. This second mutation, called a somatic mutation, is acquired during a person's lifetime and is present only in tumor cells.

Mutations of the *SDHC* gene lead to loss of SDH enzyme activity, which results in abnormal hypoxia signaling and formation of tumors.

Chromosomal Location

Cytogenetic Location: 1q23.3, which is the long (q) arm of chromosome 1 at position 23.3

Molecular Location: base pairs 161,314,376 to 161,364,751 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- C560_HUMAN
- CYB560
- CYBL
- cytochrome B large subunit of complex II
- integral membrane protein CII-3
- integral membrane protein CII-3b
- PGL3
- QPs-1
- QPS1
- SDH3
- succinate dehydrogenase complex, subunit C, integral membrane protein, 15kDa
- succinate dehydrogenase cytochrome b560 subunit, mitochondrial
- succinate-ubiquinone oxidoreducatase cytochrome B large subunit
- succinate-ubiquinone oxidoreductase cytochrome B large subunit

Additional Information & Resources

Educational Resources

- Biochemistry (5th Edition, 2002): Oxaloacetate Is Regenerated by the Oxidation of Succinate
  https://www.ncbi.nlm.nih.gov/books/NBK22427/#A2401

GeneReviews

- Hereditary Paraganglioma-Pheochromocytoma Syndromes
  https://www.ncbi.nlm.nih.gov/books/NBK1548

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SDHC%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- PARAGANGLIOMA AND GASTRIC STROMAL SARCOMA
  http://omim.org/entry/606864
- SUCCINATE DEHYDROGENASE COMPLEX, SUBUNIT C, INTEGRAL MEMBRANE PROTEIN, 15-KD
  http://omim.org/entry/602413

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/SDHCID389.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SDHC%5Bgene%5D
- HGNC Gene Family: Mitochondrial complex II: succinate dehydrogenase subunits
  http://www.genenames.org/cgi-bin/genefamilies/set/641
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10682
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6391
- UniProt
  http://www.uniprot.org/uniprot/Q99643

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https://ghr.nlm.nih.gov/gene/SDHC

Reviewed: December 2011
Published: March 21, 2017

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